

SEP 04 2009

Form PTO-1449

Attorney's Docket No.
ARR-0037-1Application Serial No.
10/578,692

Applicant(s)

Rajiv Nayar, et al.

(use several sheets if necessary)

Filing Date:
August 26, 2006Group Art Unit:
1652

U.S. PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Filing Date (if appropriate)
	1.	11/13/2003	2003/0211548	Packard, et al.			
	2.	07/25/2002	2002/0099013	Piccariello, et al.			
	3.	04/24/2003	2003/0078276	Andrianjara, et al.			
	4.	04/17/2003	2003/0073217 A1	Barr, et al.			
	5.	04/10/2003	2003/0068280	Bannister, et al.			
	6.	07/05/2001	2001/006939	Niven, et al.			
	7.	4/17/1979	4,150,071	Pecina			
	8.	4/22/1980	4,198,969	Virag			
	9.	3/3/1981	4,253,468	Lehmbeck			
	10.	11/24/1981	4,301,970	Craighero			
	11.	6/12/1984	4,453,542	Hughes			
	12.	7/8/1986	4,599,311	Kawasaki			
	13.	11/4/1986	4,620,670	Hughes			
	14.	12/8/1987	4,711,848	Insley, et al.			
	15.	03/22/1988	4,732,973	Barr, et al.			
	16.	06/01/1988	4,752,576	Brake, et al.			
	17.	10/1/1988	4,775,622	Hitzeman, et al.			
	18.	6/1/1989	4,837,148	Cregg			
	19.	6/1/1989	4,839,283	Kawasaki, et al.			
	20.	5/1/1990	4,929,555	Cregg, et al.			
	21.	6/5/1990	4,931,373	Kawasaki, et al.			
	22.	7/1/1990	4,940,661	Etcheverry, et al.			
	23.	4/1/1991	5,010,003	Chang, et al.			
	24.	5/1/1991	5,013,652	Straus berg, et al.			
	25.	3/3/1992	5,093,316	Lezdey, et al.			
	26.	5/19/2002	5,114,953	Galardy, et al.			
	27.	7/28/1992	5,134,119	Lezdey, et al.			
	28.	9/22/1992	5,150,071	Bouzidi			
	29.	11/24/1992	5,166,134	Lezdey, et al.			
	30.	6/8/1993	5,218,091	Kawasaki, et al.			
	31.	10/26/1993	5,256,657	Singh, et al.			
	32.	1/14/1997	5,594,106	Black, et al.			
	33.	4/8/1997	5,618,786	Roosdorp, et al.			
	34.	12/9/1997	5,696,147	Galardy			
	35.	6/30/1998	5,773,438	Levy, et al.			

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).



Form PTO-1449

INFORMATION DISCLOSURE STATEMENT

Attorney's Docket No.
ARR-0037-1Application Serial No.
10/578,692

Applicant(s)

Rajiv Nayar, et al.

(use several sheets if necessary)

Filing Date:
August 26, 2006Group Art Unit:
1652

	36.	07/14/1998	5,780,440	Lezdey, et al.			
	37.	4/6/1999	5,892,112	Levy, et al.			
	38.	7/1/1999	5,922,569	Heim, et al.			
	39.	10/26/1999	5,972,986	Seibert, et al.			
	40.	11/30/1999	5,993,783	Elijamal, et al.			
	41.	5/30/2000	6,068,994	Barr			
	42.	8/1/2000	6,103,500	Innis, et al.			
	43.	10/17/2000	6,133,304	Peterson, Jr., et al.			
	44.	3/1/2001	6,204,012	Hellmuth, et al.			
	45.	07/2001	6,267,958 B1	Andya, et al			
	46.	10/22/2002	6,469,040	Seibert, et al.			
	47.	12/03/2002	6,489,308 B1	Shapiro, et al.			
	48.	4/8/2003	6,544,497	Zhu, et al.			
	49.	02/17/2004	6,693,096	Fritz, et al.			
	50.	5/25/2004	6,740,655	Magee, et al.			
	51.	08/27/2009	10/579,088	Kaufman C. Office Action			
	52.	11/16/2007	11/077,276	Kam, C.M. Office Action			
	53.	07/31/2008	11/077,276	Kam, C.M. Office Action			
	54.	01/13/2009	11/077,276	Kam, C.M. Office Action			
	55.	06/05/2009	11/077,276	Kam, C. M. Office Action			

FOREIGN PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Translation	
							YES	NO
	56.	09/28/1988	EP 0 284 044	EP				
	57.	11/02/1988	EP 0 289 336	EP				
	58.	07/31/2002	EP 0 648 838	EP				
	59.	10/02/2002	EP 1 047 450	EP				
	60.	07/31/2002	EP 1 226 136	EP				
	61.	12/27/1990	EP 73,654 A	EP				
	62.	06/15/2000	WO 00/34237	WO				
	63.	07/11/2002	WO 02/053138	WO				
	64.	08/22/2002	WO 02/064080	WO				
	65.	06/27/2002	WO 02/50287	WO				
	66.	08/21/2003	WO 03/068188	WO				
	67.	09/18/2003	WO 03/075959	WO				
	68.	11/22/1984	WO 1984/04538	WO				
	69.	07/01/1999	WO 2004/103364	WO				
	70.	01/13/2005	WO 2005/003150	WO				

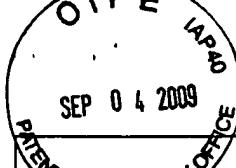
EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).

SEP 04 2009

PTO/SB/08 (2/92)
Sheet 1 of 1

Form PTO-1449

INFORMATION DISCLOSURE STATEMENT

Attorney's Docket No.

ARR-0037-1

Application Serial No.

10/578,692

Applicant(s)

Rajiv Nayar, et al.

(use several sheets if necessary)

Filing Date:
August 26, 2006Group Art Unit:
1652

71.	06/11/1992	WO 92/09282	WO
72.	06/11/1992	WO 92/09556	WO
73.	06/11/1992	WO 92/09563	WO
74.	07/22/1993	WO 93/13741	WO
75.	02/03/1994	WO 94/02446	WO
76.	09/29/1994	WO 94/21625	WO
77.	10/13/1994	WO 94/22309	WO
78.	04/13/1995	WO 95/09841	WO
79.	07/27/1995	WO 95/19965	WO
80.	05/30/1996	WO 96/16027	WO
81.	11/13/1997	WO 97/42168	WO
82.	2/26/1998	WO 98/07742	WO
83.	04/09/1997	WO 98/14424	WO
84.	10/8/1998	WO 98/43946	WO
85.	10/29/1998	WO 98/47863	WO
86.	09/10/1999	WO 99/44989	WO

OTHER DOCUMENTS

(including author, title, date, pertinent pages, etc.)

Examiner Initials	Ref. No.	Title
	87.	Ash, M., et al., Handbook of Pharmaceutical Additives, 2nd Edition, Synapse Information Resources, Inc., pp. 797-798, 2002.
	88.	Barnes, P.J., "Novel Approaches and Targets for Treatment of Chronic Obstructive Pulmonary Disease," <i>Am.J. Respir. Crit. Care Med.</i> , 160:S72-S79, 1999.
	89.	Broach, et al., "Transformation in Yeast: Development of a Hybrid Cloning Vector and Isolation of the CAN1 Gene," <i>Gene</i> , 8:121-133, 1979.
	90.	Carlson, J.A., et al., "Accumulation of PiZ α_1 -Antitrypsin Causes Liver Damage in Transgenic Mice," <i>J. Clin. Invest.</i> , 83:1183-1190, 1989.
	91.	Carpenter, J.F., et al., "Rational Design of Stable Lyophilized Protein Formulations: Theory and Practice, Rational Design of Stable Protein Formulations Theory and Practice," <i>13</i> : 109-133, 2002.
	92.	Carrell, R.W., et al., Structure and Variation of Human Alpha 1-Antitrypsin," <i>Nature</i> , 298: 329-334, 1982.
	93.	Carter, P., et al., "Improved Oligonucleotide Site-Directed Mutagenesis Using M13 Vectors," <i>Nucleic Acids Research</i> , 13(12): 4431-4443, 1985.
	94.	Churg, et al., "Proteases and Emphysema," <i>Current Opinion in Pulmonary Medicine</i> , 11: 153-159, 2005.
	95.	Cregg, et al., "Pichia Pastoris as a Host System for Transformations," <i>Molecular and Cellular Biology</i> , 5(12): 3376-3385, 1985.

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).

SEP 04 2009

PTO/SB/08 (2/92)
Sheet 1 of 1

Form PTO-1449 INFORMATION DISCLOSURE STATEMENT		Attorney's Docket No. ARR-0037-1	Application Serial No. 10/578,692
		Applicant(s)	Rajiv Nayar, et al.
<i>(use several sheets if necessary)</i>		Filing Date: August 26, 2006	Group Art Unit: 1652
96.	Das, et al., "Transformation of Kluyveromyces Fragilis," <i>Journal of Bacteriology</i> , <u>158</u> (3): 1165-1167, 1984.		
97.	Davidow, L.S., et al., "Integrative Transformation of the Yeast Yarrowia lipolytica," <i>Current Genetics</i> , <u>10</u> : 39-48, 1985.		
98.	Dayhoff, et al., "A Model of Evolutionary Change in Proteins," <i>Atlas of Protein Sequence and Structure</i> , National Biomedical Research Foundation, <u>5</u> (3):345-358, 1979.		
99.	De Louvencourt, et al., "Transformation of Kluyveromyces lactic by Killer Plasmid DNA," <i>Journal of Bacteriology</i> , <u>154</u> (2): 737-742, 1983.		
100.	du Preez, J.C., et al., "Transcriptional Repression of ADH2-Regulated β-xylanase Production by Ethanol in Recombinant Strains of Saccharomyces Cerevisiae," <i>FEMS Yeast Research</i> , <u>1</u> : 233-240, 2001.		
101.	Dycaico, et al., "Neonatal Hepatitis Induced by α ₁ -Antitrypsin: A Transgenic Mouse Model," <i>Science</i> , <u>242</u> : 1409-1412, 1988.		
102.	European Search Report dated January 9, 2007.		
103.	Gadek, et al., "α ₁ -Antitrypsin Deficiency," <i>The Metabolic Basis of Inherited Disease</i> , Stanbury, J.B. et al., eds., McGraw-Hill, New York, pp. 1450-1467, 1982.		
104.	Gaillardin, et al., "Integrative transformation of the Yeast Yarrowia lipolytica," <i>Current Genetics</i> , <u>10</u> : 49-58, 1985.		
105.	Colau, B., et al., "Revised sequence of full-length complementary DNA coding for human alpha 1-antitrypsin" as disclosed (1984), GenBank Accession No. AAB59375, Host: NCBI, Database: Genbank.		
106.	Gleeson, M.A., et al., "Transformation of the Methylotrophic Yeast Hansenula polymorpha," <i>Journal of General Microbiology</i> , <u>132</u> : 3459-3465, 1986.		
107.	Hein, J. "Unified Approach to Alignment and Phylogenies," <i>Methods in Enzymology</i> , <u>183</u> : 626-645, 1990.		
108.	Hercz, A., "Proteolytic Cleavages in Alpha-One Antitrypsin and Microheterogeneity," <i>Biochem. Biophys. Res. Comm.</i> , <u>128</u> (1): 199-203, 1985.		
109.	Higgins, D.G., et al., "Fast and Sensitive Multiple Sequence Alignments on a Microcomputer," <i>CABIOS Communications</i> , <u>5</u> (2): 151-153, 1989.		
110.	Hinnen, A., et al., "Transformation of Yeast," <i>Proc. Natl. Acad. Sci. USA, Genetics</i> , <u>75</u> (4): 1929-1933, 1978.		
111.	Huang, et al., "Expression and Purification of Functional Human Alpha1-Antitrypsin from Cultured Plant Cells," <i>Biotechnology Prog</i> , <u>17</u> : 126-33, 2001.		
112.	Hunnighake, G.W., et al., "Cigarette Smoking and Lung Destruction: Accumulation of Neutrophils in the Lungs of Cigarette Smokers," <i>Am. Rev. Respir. Dis.</i> , <u>128</u> : 833-838, 1983.		
113.	Ito, H., et al., "Transformation of Intact Yeast Cells Treated with Alkali Cations", <i>Journal of Bacteriology</i> , <u>153</u> (1): 163-168, 1983.		
114.	Jennings, Thomas A., "Lyophilization: Introduction and Basic Principles," Interpharm Press, pp. 42-44, 261-279, 1999.		
115.	Jones, E.W., "Tackling the Protease Problem in Saccharomyces Cerevisiae," <i>Methods in Enzymology</i> , <u>194</u> : 428-453,		

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).

O P I E
SEP 04 2009
PATENT INFORMATION DISCLOSURE STATEMENT

Form PTO-1449 PATENT INFORMATION DISCLOSURE STATEMENT		Attorney's Docket No. ARR-0037-1	Application Serial No. 10/578,692
		Applicant(s)	Rajiv Nayar, et al.
<i>(use several sheets if necessary)</i>		Filing Date: August 26, 2006	Group Art Unit: 1652
116.	Jones, E.W., "Vacuolar Proteases in Yeast <i>Saccharomyces Cerevisiae</i> ," <i>Methods in Enzymology</i> , 85(31):372-386, 1990.		
117.	Kaslow, D.C., et al., "Production, Purification and Immunogenicity of a Malaria Transmission-Blocking Vaccine Candidate: TBV25H Expressed in Yeast and Purified Using Nickel-NTA Agarose," <i>Nature Publishing Group</i> , 12: 494-499, 1994.		
118.	Kunze, et al., "Transformation of the Industrially Important Yeasts <i>Candida maltosa</i> and <i>Pichia guilliermondii</i> ," <i>Journal of Basic Microbiology</i> , 25(2): 141-144, 1984.		
119.	Kurachi, K., et al., "Cloning and Sequence of cDNA Coding for α_1 -Antitrypsin," <i>Proc Natl Acad Sci USA, Biochemistry</i> , 78(11): 6826-6830, 1981.		
120.	Kurjan, J., et al., "Structure of a Yeast Pheromone Gene (MF α): A Putative α -Factor Precursor Contains Four Tandem Copies of Mature α -Factor," <i>Cell</i> , 30: 933-943, 1982.		
121.	Kurtz, M.B., et al., "Integrative Transformation of <i>Candida albicans</i> , Using a Cloned <i>Candida ADE2</i> Gene," <i>Molecular and Cellular Biology</i> , 6(1): 142-149, 1986.		
122.	Ljujic, et al., "Screening of alpha-1-antitrypsin gene by denaturing gradient gel electrophoresis (DGGE)", <i>J. Biochem. Biophys. Meth.</i> , 68(3) 167-173, (2006)		
123.	Lomas, D.A., et al., "The Mechanism of Z α_1 -Antitrypsin Accumulation in the Liver," <i>Nature</i> , 357: 605-607, 1992.		
124.	Luisetti, et al., "Alpha-1-antitrypsin deficiency 1: Epidemiology of alpha 1-antitrypsin deficiency", <i>Thorax</i> , 59 (2): 164-169, (2004)		
125.	Myers, E.W., et al. "Optimal Alignments in Linear Space," <i>CABIOS Communications</i> , 4(1): 11-17, 1988.		
126.	Nail, S., et al., "Development and Manufacture of Protein Pharmaceuticals," <i>Pharmaceutical Biotechnology</i> , 14: 65-66, 2002.		
127.	Neddeleman, S.B., et al., "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," <i>J. Mol. Biol.</i> , 48: 443-453, 1970.		
128.	Noronha, S.B., et al., "Transition Phase in the Production of Recombinant Proteins in Yeast Under the ADH2 Promoter: An Important Step for Reproducible Manufacturing of a Malaria Transmission Blocking Vaccine Candidate," <i>Journal of Individual Microbiology & Biotechnology</i> , 20:192-199, 1998.		
129.	O'Connor, G.M., "Design and Evaluation of Control Strategies for High Cell Density Fermentations," <i>Biotechnology and Bioengineering</i> , 39 (3):293-304, 1992.		
130.	Pemberton, P., et al., "Inhaled recombinant Alpha 1-Antitrypsin Ameliorates Cigarette Smoke-Induced Emphysema in the Mouse," <i>COPD: Journal of Chronic Obstructive Pulmonary Disease</i> , 3: 101-108, 2006.		
131.	Rabe, "Outcome Measures in COPD," <i>Primary Care Respiratory Journal</i> , 13: 177-178, 2004.		
132.	Randolph, T.W., et al., "Surfactant-Protein Interactions," <i>Rational Design of Stable Protein Formulations: Theory and Practice, Pharmaceutical Biotechnology</i> , Kluwer Academic/Plenum Publishers, pp. 159-175, 2002.		
133.	Robinson, D.F., "Comparison of Labeled Trees with Valency Three," <i>Journal of Combinatorial Theory</i> , 11: 105-119, 1971.		
134.	Roche, N., et al., "Current Issues in the Management of Chronic Obstructive Pulmonary Diseases," <i>Respirology</i> , 2: 215-229, 1997.		

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).

SEP 04 2008

PTO/SB/08 (2/92)
Sheet 1 of 1

Form PTO-1449

INFORMATION DISCLOSURE STATEMENT

Attorney's Docket No.
ARR-0037-1Application Serial No.
10/578,692

Applicant(s)

Rajiv Nayar, et al.

(use several sheets if necessary)

Filing Date:
August 26, 2006Group Art Unit:
1652

	135.	Roggenkamp, R., et al., "Transformation of the Methylotrophic Yeast Hansenula polymorpha by Autonomous Replication and Integration Vectors," <i>Mol. Gen. Genet.</i> , <u>202</u> : 302-308, 1986.
	136.	Rosenerg, et al., "Synthesis in Yeast of a Functional Oxidation-Resistant Mutant of Human Alpha1-Antitrypsin," <i>Nature</i> , <u>312</u> : 77-80, 1984.
	137.	Sabin, E.A., et al., "High-Level Expression and in Vivo Processing of Chimeric Ubiquitin Fusion Proteins in <i>Saccharomyces Cervisiae</i> ," <i>Bio/Technology</i> , <u>7</u> : 705-709, 1989.
	138.	Saitou, N., et al., "The Neighbor-Joining Method: A new Method for Reconstructing Phylogenetic Trees," <i>Molecular Biology and Evolution</i> , pp. 406-425, 1987.
	139.	Schasteen, C.S., et al., "Synthetic Peptide Inhibitors of Complement Serine Proteases - Significant Increase in Inhibitor Potency Provides Further Support for the Functional Equivalence Hypothesis," <i>Molecular Immunology</i> , <u>28</u> (1/2): 472-479, 1991.
	140.	Schiestl, et al., "High Efficiency Transformation of Intact Yeast Cells Using Single Stranded Nucleic Acids as a Carrier," <i>Current Genetics</i> , <u>16</u> : 339-346, 1989.
	141.	Shapiro, "Evolving Concepts in the Pathogenesis of Chronic Obstructive Pulmonary Disease," <i>Clinics in Chest Medicine</i> , <u>21</u> (4):621-632, 2000.
	142.	Smith, et al., "Pulmonary Deposition and Clearance of Aerosolized Alpha-1-Proteinase Inhibitor Administered to Dogs and to Sheep," <i>J. Clin. Invest.</i> , <u>84</u> : 1145-1154, 1989.
	143.	Smith, T.F., et al., "Comparison of Biosequences," <i>Adv. in Appl. Math.</i> , <u>2</u> : 482-489, 1981.
	144.	Stockley, et al., "Therapeutic Efficacy of Alpha-1 Antitrypsin (AAT) Augmentation Therapy on the Loss of Lung Tissue: An Integrated Analysis," <i>European Respiratory Society</i> , Abstract, 2008.
	145.	Stolk, et al., "Progression Parameters for Emphysema: A Clinical Investigation," <i>Respiratory Medicine</i> , <u>101</u> : 1924-1930, 2007.
	146.	Terashima, et al., "Production of Functional Human Alpha1-Antitrypsin by Plant Cell Culture," <i>Appl. Microbiol. Biotechnol.</i> , <u>52</u> : 516-523, 1999.
	147.	Travis, et al., "Isolation and Properties of Recombinant DNA Produced Variants of Human Alpha1-Proteinase Inhibitor," <i>Journal of Biological Chemistry</i> , <u>260</u> (7): 4384-4389, 1985.
	148.	Tuite, M.F., et al., "Regulated High Efficiency Expression of Human Interferon-Alpha in <i>Saccharomyces cerevisiae</i> ," <i>The EMBO Journal</i> , <u>1</u> (5): 603-608, 1982.
	149.	Van Den Berg, et al., "Kluyveromyces as a Host of Heterologous Gene Expression: Expression and Secretion of Prochymosin," <i>Biotechnology</i> , <u>8</u> : 135-140, 1990.
	150.	Van Steenbergen, "Alpha 1-antitrypsin deficiency: an overview," <i>Acta. Clin. Belg.</i> , <u>48</u> (3): 171-189, (1993)
	151.	Wells, J.A., "Cassette Mutagenesis: An Efficient Method for Generation of Multiple Mutations at Defined Sites, et al., <i>Gene</i> , <u>34</u> : 315-323, 1985.
	152.	Wells, J.A., et al., "Importance of Hydrogen-Bond Formation in Stabilizing the Transition State of Sutilisin," <i>Philos Trans. R. Soc. London</i> , <u>317</u> : 415-423, 1986.
	153.	Wilbur, W.J., et al., "Rapid Similarity Searches of Nucleic Acid and Protein Data Banks," <i>Proc Natl Acad of Sci USA</i> , <u>80</u> :

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).

SEP 04 2009

Form PTO-1449

Attorney's Docket No.
ARR-0037-1Application Serial No.
10/578,692

INFORMATION DISCLOSURE STATEMENT

Applicant(s)

Rajiv Nayar, et al.

(use several sheets if necessary)

Filing Date:
August 26, 2006Group Art Unit:
1652

726-730, 1983.

154. Winkler, M., "Time-Profiling and Environmental Design in Computer -Controlled Fermentation and Enzyme Production," Genetically-Engineered Proteins and Enzymes from Yeast: Production Control, Ellis Horwood Limited, Chp. 4 and 5, pp. 96-184, 1991.

155. Wu, Y., et al., "A Lag in Intracellular Degradation of Mutant α 1-Antitrypsin Correlates with the Liver Disease Phenotype in Heterozygous PiZZ α 1-Antitrypsin Deficiency," Proc. Natl. Acad. Sci., 91: 9014-9018, 1994.156. Zekian, V.A., et al., "Construction, Replication, and Chromatin Structure of TRP1 R1 Circle, a Multiple-Copy Synthetic Plasmid Derived from *Saccharomyces cerevisiae* Chromosomal DNA", Molecular and Cellular Biology, 2(3): 221-232, 1982.

157. Zoller, et al., "Oligonucleotide-Directed Mutagenesis Using M13-Derived Vectors: An Efficient and General Procedure for the Production of Point Mutations in any Fragment of DNA," Nucleic Acids Research, 10(20): 6487-6500, 1982.

158. Zou, et al., "Maspin, a Serpin with Tumor-Suppressing Activity in Human Mammary Epithelial Cells," Science, 263: 526-529, 1994.

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

*If an asterisk is placed beside the reference number, a copy is not provided because the reference was previously cited by or submitted to the PTO in a prior application that is identical in the statement and relied upon for an earlier filing date under 35 U.S.C. §120. 37 C.F.R. §1.98 (d).